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Assessment of pharyngeal motor function using a novel velopharyngeal squeeze maneuver and a novel endoscopic pharyngeal contraction grade scale in patients with dysphagia after radiotherapy for nasopharyngeal carcinoma

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Abstract

Background: To investigate a novel velopharyngeal squeeze maneuver (VPSM) and novel endoscopic pharyngeal contraction grade (EPCG) scale for the evaluation of pharyngeal motor function.

Methods: During endoscopic examination of 77 post-irradiated nasopharyngeal carcinoma patients and control subjects, VPSM was rated and lateral pharyngeal wall movement graded with EPCG scale during swallowing. Pharyngeal constriction ratio (PCR) measured by videofluoroscopy was used for correlation.

Results: VPSM and EPCG scale showed almost perfect intra-rater and inter-rater reliability (Kappa: >0.90). VPSM was present in 61% of patients suggesting good pharyngeal motor function. VPSM was predictive of EPCG scale (Wald statistic = 29.99, $p < 0.001$). EPCG scale also correlated strongly with PCR (r: 0.812) and was predictive for aspiration (odds ratio: 22.14 [95% CI 5.01–97.89, $p < 0.001$]).

Conclusions: VPSM and EPCG scale are two novel tools to assess pharyngeal motor function, and both correlate well with pharyngeal contractility and aspiration.

KEYWORDS

dysphagia, endoscopy, nasopharyngeal carcinoma, pharyngeal motor function, pharyngeal squeeze

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1 | INTRODUCTION

Nasopharyngeal carcinoma is endemic in south-eastern Asia, the region with the highest incidence in the world.[1] Globally, 129 079 new cases of nasopharyngeal carcinoma and 72 987 deaths from nasopharyngeal carcinoma were reported in 2018.[1] During the same year, the incidence of nasopharyngeal carcinoma in Hong Kong was 18.6 per 100 000 males and 4.9 per 100 000 females.[2] The mainstay of treatment for this malignancy is radiotherapy with or without chemotherapy, in which advances have resulted in disease control and survival rates improving over the recent decade.[3,4] Due to increasing longevity, survivors are now suffering longer-term side effects and complications of treatment such as dysphagia due to post-irradiation sensory and motor neuropathies and soft tissue fibrosis.[5–7] This is an important cause of dysphagia in the south-eastern Asian population.[8–11]

We have previously shown that impaired pharyngeal contraction correlates with penetration and aspiration in post-irradiated nasopharyngeal carcinoma patients.[12,13] The gold standard to measure pharyngeal contraction is high-resolution pharyngeal manometry, but the setup is expensive and specially trained staffs are needed to perform it and interpret the results.[14,15] Bastian described the pharyngeal squeeze maneuver (PSM) as a standard assessment tool used during an endoscopic pharyngeal evaluation to look for weakness or paralysis of the pharyngeal constrictors in a western white population, where it has been widely used.[16] A presence of PSM is highly predictive of intact pharyngeal strength and function.[17] However, the PSM is inconsistent in its ability to predict pharyngeal contraction in a Chinese population.

It has been our observation that the PSM is almost universally absent in our Chinese subjects. However, the excursion of the lateral wall of the velopharyngeal port, which we describe as the velopharyngeal squeeze maneuver (VPSM), is present in normal Chinese subjects during phonation of a high pitch vowel. The VPSM is potentially a more useful clinical sign to assess pharyngeal motor function than the PSM and, hence, forms one hypothesis of this study. In the field of flexible endoscopic evaluation of swallowing (FEES), only the pharyngeal squeeze and the "white-out" sign, a flash of white related to the decreasing distance between pharyngeal tissue and the light source during swallowing, are used to indicate or imply either present and thus normal or an absent and thus abnormal pharyngeal contractility.[18,19]

There is a need first for a more consistent and ultimately reproducible surrogate to assess pharyngeal contraction, other than the pharyngeal squeeze maneuver, especially in Chinese subjects, and second for a more sensitive graded assessment tool of pharyngeal contraction impairment, other than a dichotomous "present" or "absent. In addition, a grading scale of pharyngeal contraction that also indicates a "mild," "moderate," or "severe" level of impairment will be a better guide of the swallowing ability of patients, which, in turn, will have implications for swallowing management and outcomes. The hypothesis of this study is that a novel VPSM and a novel endoscopic pharyngeal contraction grade (EPCG) scale can quantify the pharyngeal contraction or motor function of patients using a pharyngeal constriction ratio (PCR) that is a derivative of a videofluoroscopic swallowing study (VFSS) as a gold standard of pharyngeal function measurement. We tested the inter-rater and intra-rater reliability to determine if the grading of the VPSM and the EPCG scale was reproducible and consistent between users.

2 | MATERIALS AND METHODS

2.1 | Subject recruitment and data collection

A multicenter cohort study was conducted at the Prince of Wales, United Christian and Tseung Kwan O Hospitals, which are tertiary referral centers for otolaryngology and head and neck surgery in Hong Kong. This study was reviewed and approved by the Institutional Review Boards of the New Territories East Hospital Cluster (CREC 2014-391) and Kowloon East Hospital Cluster (KC/KE-14-0173/FR-1), respectively, which oversee all research activities in the participating institutions.

Patients with symptoms of dysphagia and a history of nasopharyngeal carcinoma treated with radiotherapy who were referred from the three hospitals to the combined Dysphagia Clinic at the Prince of Wales Hospital between January 2015 and January 2016 were recruited. Patients with a history of primary nasopharyngeal carcinoma treated with radiotherapy or chemo-radiotherapy and at least 12 months of follow-up were included in the study. Cerebral vascular accident, head and neck abscess, other acute causes of dysphagia, unilateral pharyngeal or vocal cord paralysis, or both were exclusion criteria.

2.2 | Flexible endoscopic evaluation of swallowing or FEES

Each patient underwent a FEES by the senior otolaryngologist and Dysphagia Clinic chief (PK). A speech therapist (speech-language pathologist) with over 10 years' experience in the assessment and management of dysphagia patients was also in attendance. The FEES was performed

using a 4.2 mm fiberoptic endoscope (FNL-10RAP, Pentax Corporation, Tokyo, Japan), a halogen light source (LH-150PC, Pentax Corporation, Tokyo, Japan), an endoscopic camera (PSV-4000, Pentax Corporation, Tokyo, Japan), and a video monitor (PVM-20M2MDU, Sony Trinitron, Japan) and was watched by both the senior otolaryngologist and speech therapist. The nasal cavity, nasopharynx, oropharynx, laryngopharynx, and larynx were inspected for any structural abnormalities.

The tip of the endoscope was then withdrawn from the oropharynx into the postnasal space, to a position adjacent to the posterior free margin of the nasal septum, so that the nasopharynx including both Eustachian tube cushions could be seen. The patient was asked to perform a VPSM by the forceful phonation of a high pitched "ee" sound in which the endoscopist looked for medial movement of the lateral velopharyngeal wall toward the midline and posterior movement of the soft palate toward the posterior pharyngeal wall. A present VPSM was defined as any attempt of the lateral walls of the velopharynx to medialize during phonation, in which an absent VPSM was defined as no attempted medialization movement of

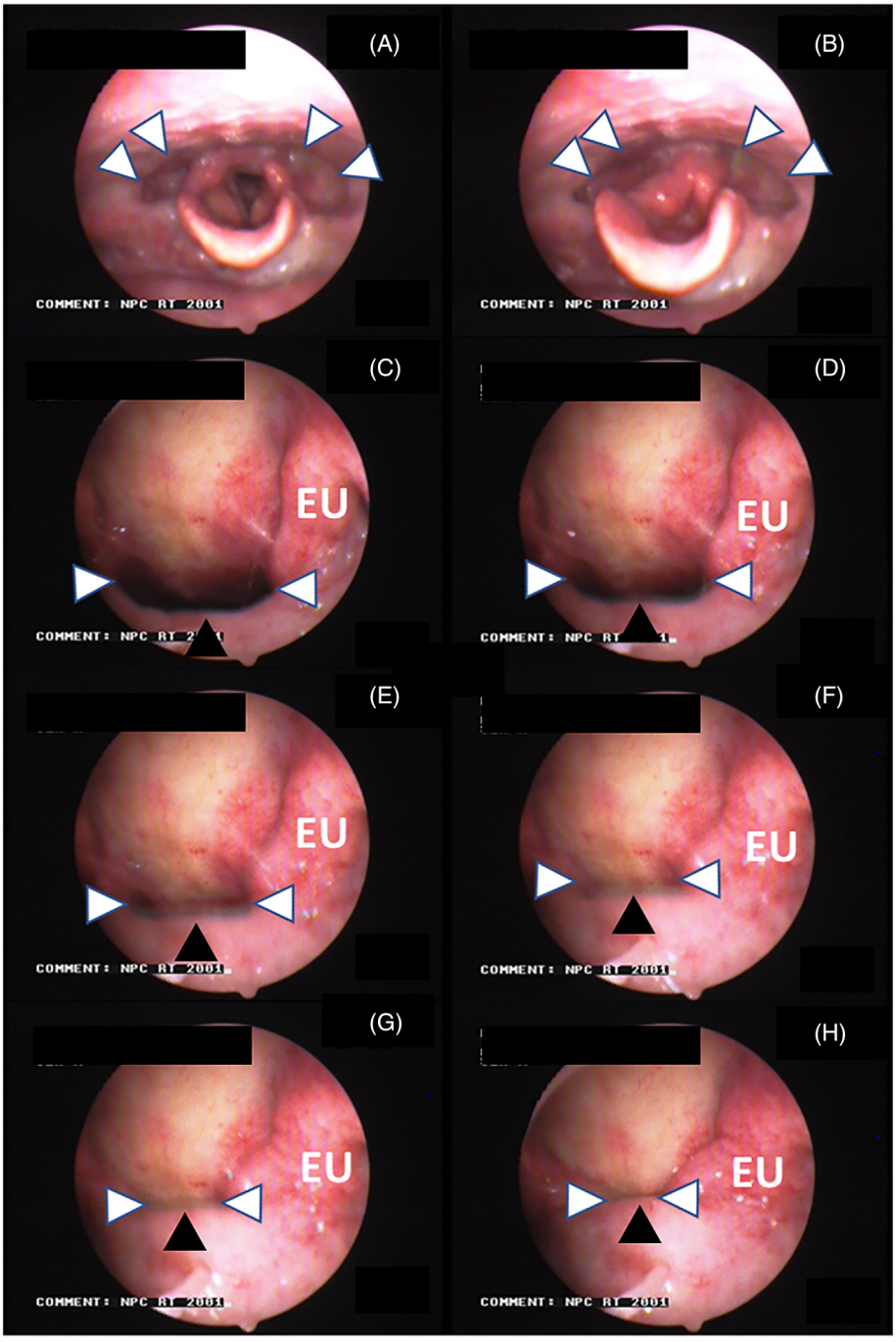

FIGURE 1 Pharyngeal squeeze maneuver (PSM) and velopharyngeal squeeze maneuver (VPSM) in a post-irradiated nasopharyngeal carcinoma patient. (A) The appearance of the pyriform fossae at rest in relation to the lateral pharyngeal wall (white arrows) and aryepiglottic fold. (B) Lack of medial movement of the lateral pharyngeal wall during the pharyngeal squeeze maneuver. Note that the vocal cords are adducted during a forceful and high pitch "ee." (C–H) VPSM with gradual medialization of the lateral wall of the velopharynx (white arrows) and the posterior movement of the soft palate (black arrow). The velopharynx is closed during a forceful and high pitch "ee" (EU: Eustachian tube) [Color figure can be viewed at wileyonlinelibrary.com]

the lateral walls of the velopharynx during phonation. (Figure 1C–H).

The tip of the endoscope was then advanced and positioned at the junction of the lower nasopharynx and upper oropharynx, just posterior to the level of the lower soft palate, which allows visualization of the entire laryngeal inlet and hypopharynx and observation of swallowing without touching mucosa of the oropharynx, which can cause a gag reflex. The patient was asked to perform a PSM by the forceful phonation of a high pitched "ee" sound for at least half but ideally for one full expiration, and the endoscopy recorded. A present PSM was the medialization of the lateral hypopharyngeal wall on either side to abut the aryepiglottic (AE) fold (Figure 2), in which an absent PSM was the lack of abutment or contact (Figure 1A,B).

With the endoscope still in the same position, each patient was given a 5 ml bolus of a thin liquid (IDDSI[20] level 1) and then a 5 ml bolus of a thick liquid (IDDSI level 2) to swallow with three swallow attempts allowed for each bolus, and the endoscopy recorded. The degree of movement of the lateral pharyngeal wall during the swallow was graded according to the five-point EPCG scale (Table 1) during the pharyngeal phase of the swallow **(**Figure 3**)**. The pharyngeal phase of swallowing was rated for the amount of food residue in the valleculae, in the pyriform fossae, for penetration and for aspiration of food material into the larynx and trachea. Abnormalities were scored if they were present on two of the three swallowing attempts. Rosenbeck's penetration–aspiration scale (PAS)[21] and the Yale pharyngeal residue severity scale[22] were used to grade the swallowing outcome. The procedure was recorded with a video-capture device (AVerMedia technologies Inc., Taipei, Taiwan) at a video-capture rate of 30 frames/s as an MPEG-2 video format and stored on the hard disk of a secure desktop computer for later review, interpretation, and analysis.

2.3 | Videofluoroscopic study of swallowing or VFSS

A videofluoroscopic study of swallowing was performed using a fluoroscopy suite (Siemens Artis Zee Multi-Purpose System, Siemens health care GmbH, Erlangen, Germany) equipped with a DVD recorder. Examinations were performed by a speech therapist (speech-language pathologist) and radiologist experienced in the assessment and management of dysphagia patients and blinded to the findings of the FEES examination. During a VFSS, 5 ml of thin liquid barium (200 ml water mixed with 40 ml barium powder) and then 5 ml of thick liquid barium (100 ml water mixed with 10 ml barium powder and 15 ml thickener) were given to the patient to swallow in three attempts. The thin liquid swallow was repeated three times. Lateral projection images with a frame rate of 15 images/s were recorded onto a DVD.

The presence or absence of penetration and aspiration was recorded. If present, the severity of the penetration and/or aspiration was rated by common consensus between the speech therapist and the radiologist using Rosenbeck's PAS.

The video files of the VFSS were subsequently evaluated by the senior otolaryngologist, who was not present during the VFSS and who was blinded to the subject's name, other identifiers and swallowing condition, and

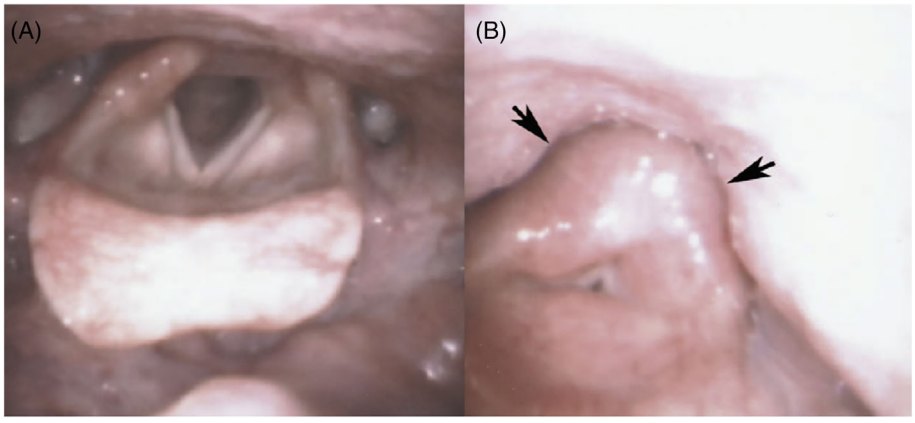

FIGURE 2 Pharyngeal squeeze maneuver (PSM) in a normal subject. (A) The appearance of the pyriform fossae at rest in relation to the lateral pharyngeal wall and aryepiglottic fold. (B) Medial movement of the lateral pharyngeal walls (black arrows) abutting the arytenoids and aryepiglottic folds during the pharyngeal squeeze maneuver. [Used with permission. Reprinted by permission from SAGE Publications: Otolaryngology—Head and Neck Surgery. Validation of the pharyngeal squeeze maneuver. Fuller SC, Leonard R, Aminpour S, et al. *Otolaryngol Head Neck Surg* 2009; 140:391–4.] [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Endoscopic pharyngeal contraction grade scale

Grade	Degree of movement of the lateral pharyngeal wall	Possible observation from the lower nasopharynx
Normal contraction	Medialization of the lateral pharyngeal wall completely obscuring the laryngeal inlet	Complete white out
Mild impairment of contraction	Medialization of lateral pharyngeal wall, abutting the aryepiglottic fold, and almost but not totally obscuring the laryngeal inlet	Partial white out and only a slit of laryngeal inlet seen
Moderate impairment of contraction	Medialization of lateral pharyngeal wall, abutting the aryepiglottic fold, but only partially obscuring the laryngeal inlet	Part or most of the laryngeal inlet is seen, but neither pyriform fossae are seen
Severe impairment of contraction	Medialization of lateral pharyngeal wall, but not able to abut the aryepiglottic fold	The entire laryngeal inlet is seen, as well as only part of one or both pyriform fossae
Absent contraction	No medialization of the lateral pharyngeal wall	The entire laryngeal inlet is seen, as well as both pyriform fossae

the PCR calculated. This is an objective calculation that aims to remove rater bias. The PCR is a well-established and widely used research tool to evaluate pharyngeal motor function, which has been validated by pharyngeal manometry.[23] The ratio is obtained by dividing the pharyngeal area visible on the lateral radiographic view at the point of maximum pharyngeal contraction during a swallow by the area in a relaxed state just before swallowing 5 ml of liquid on hold in the oral cavity. ImageJ software (NIH and LOCI, University of Wisconsin, Madison, WI, USA) was used to calculate the PCR value by estimating the cross-sectional area of the pharynx from still images captured from the video clips of the VFSS during the two pharyngeal phases of swallowing (Figure 4). The PCR value of each of the three 5 ml thin liquid bolus swallows was averaged to get a mean PCR for the three swallows. Patients with poor pharyngeal contraction during swallowing have a PCR value approaching 1, in which patients with good pharyngeal contraction have a PCR value approaching 0. A normal PCR value would not be expected to exceed 0.25 when a corresponding pharyngeal clearing pressure is greater than 60 mm Hg in a fluoroscopic and manometric study.[24]

Finally, the PCR was used as the gold standard for correlation with the pharyngeal motor function rated by the PSM, VPSM, and the EPCG scale.

2.4 | Testing of consistency for rating of pharyngeal motor function and swallowing parameters

All FEES video clips were rated separately by the senior otolaryngologist and two senior residents specializing in otolaryngology—head and neck surgery for the PSM, VPSM, EPCG scale, and Yale pharyngeal residue severity scales, which rates residue location (vallecula and pyriform sinus) and amount (none, trace, mild, moderate, and severe) and PAS, on two separate occasions, which tested intra-rater and inter-rater reliability. They were blinded by the clinical condition of the subjects and the scoring of the VFSS. Both residents were instructed in the principles of grading the PSM, VPSM, EPCG scale, Yale pharyngeal (vallecula and pyriform fossa) residue severity scale, and PAS, and then evaluated a sample of cases under the supervision of the senior otolaryngologist, to ensure their understanding of their task and the quality of their ratings. There were six ratings by three raters for each subject in this study who scored the PSM, VPSM, ECPG, Yale pharyngeal residue severity scale, and PAS. The final score for each variable for each subject was determined by the majority score out of the six ratings. If no score was the majority for each particular rating, an average score was estimated as the final score, or the senior rater decided the final score for categorical variables (e.g., PSM and VPSM) if equivocal.

2.5 | Data and statistical analysis

All statistical analyses were performed using SPSS version 23.0 (IBM, Armonk, NY, USA). Intraclass correlation coefficient (ICC) with a two-way mixed effects model and absolute agreement was computed to test the agreement of the average of the three measured PCR values for each subject by a single rater. The inter-rater and intra-rater reliability of EPCG, PAS, and scores of vallecular and pyriform residue using the

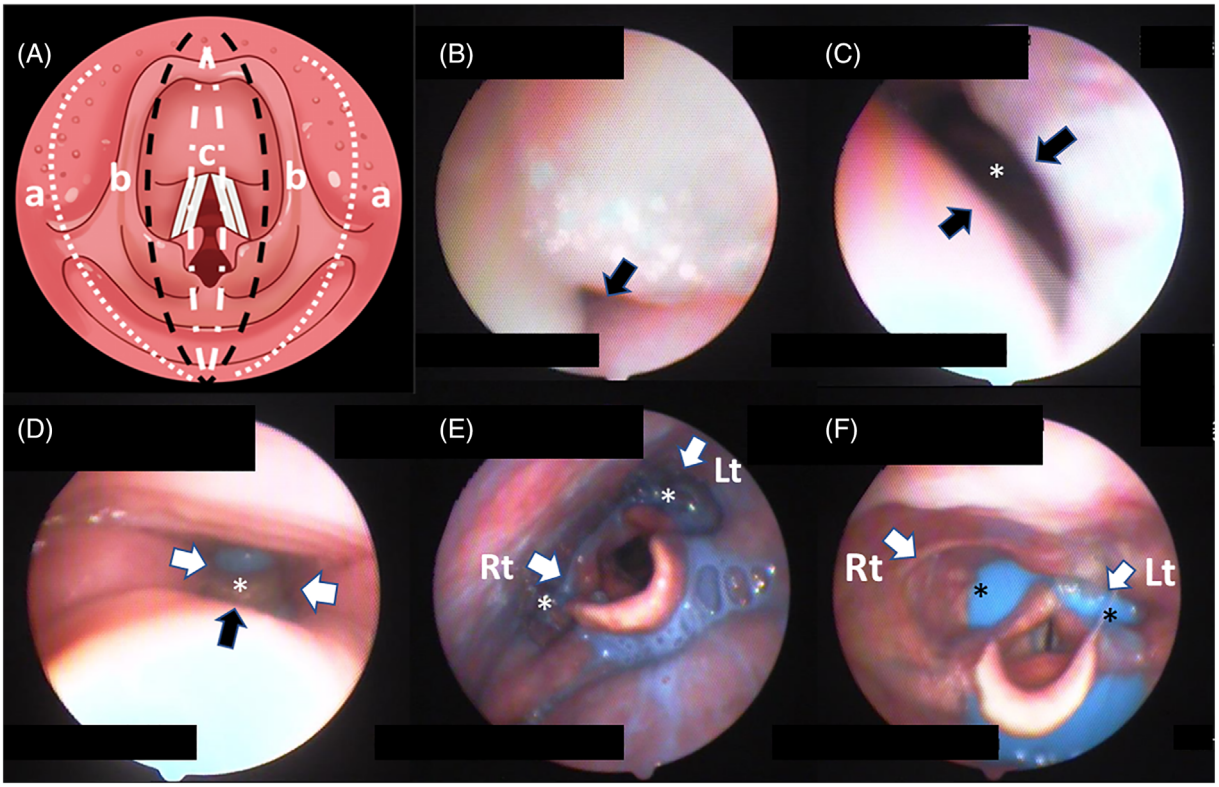

FIGURE 3 Endoscopic pharyngeal contraction grade scale. (A) A drawing of the laryngeal inlet and hypopharynx. The dotted lines (a–c) indicate the different degrees of medial movement of the lateral pharyngeal wall, indicating different degrees of lateral pharyngeal wall contraction impairment [(a) severe impairment, (b) moderate impairment, and (c) mild impairment]. (B) The "white-out" phenomenon. The residual velopharyngeal aperture (black arrow) is completely closed in a complete "white-out." (C) Mild impairment of pharyngeal wall contraction with incomplete lateral wall approximation (black arrows), but the laryngeal inlet is not well visualized. (D) Moderate impairment of pharyngeal wall contraction (white arrows) with partial visualization of the laryngeal inlet but not of the pyriform fossae. The soft palate (black arrow) moves posteriorly but is never able to abut with the posterior pharyngeal wall (P). (E) Severe impairment of pharyngeal wall contraction (white arrows) with the entire laryngeal inlet seen but not the pyriform fossae on the right (Rt) side. There is severe impairment of soft palate elevation and stasis of thin liquid (blue color) in both pyriform fossae (*). The left (Lt) pharyngeal wall of the pyriform fossa was failed to abut the aryepiglottic fold (AE) and was also rated severe impairment (F): Absent pharyngeal wall contraction on the right (Rt) pyriform fossa (white arrows) and severe impairment of the left (Lt) pharyngeal wall failed to abut the AE fold on both sides with the entire laryngeal inlet and pyriform fossae (*) seen during the endoscopic examination of swallowing. There is severe impairment of soft palate elevation and severe stasis of thin liquid (blue color) in both pyriform fossae [Color figure can be viewed at wileyonlinelibrary.com]

Yale pharyngeal residue severity rating scale were also tested using the ICC. The interpretation of ICC was based on the publication by Koo and Li,[25] in which the values of ICC < 0.5, 0.5–0.75, 0.76–0.9, and >0.9 represent poor, moderate, good, and excellent reliability, respectively.

Kappa coefficients were used to estimate the inter-rater and intra-rater reliability of binary variables, such as PSM and VPSM. The interpretation of the Kappa coefficient was based on the publication by McHugh,[26] in which the values of Kappa 0–0.2, 0.21–0.39, 0.40–0.59, 0.60–0.79, 0.80–0.90, and >0.9 represent none, minimal, weak, moderate, strong, and almost perfect agreement, respectively.

Point-biserial and Pearson's correlation coefficients were used to determine the relationship of the PCR to the VPSM and EPCG scale, respectively ($\sigma > 0.5$ is a large correlation).

The Mann-Whitney *U* test was used to test the difference of PCR and vallecular/pyriform residue scores between the two categories of VPSM. The Kruskal-Wallis test was used to analyze the difference in PCR values among various EPCG gradings, and vallecular/pyriform residue ratings among the EPCG gradings.

Ordinal logistic regression was used to analyze the association between VPSM and EPCG, VPSM and vallecular/pyriform residue scores, and EPCG and vallecular/pyriform residue scores. Odds ratio was computed for

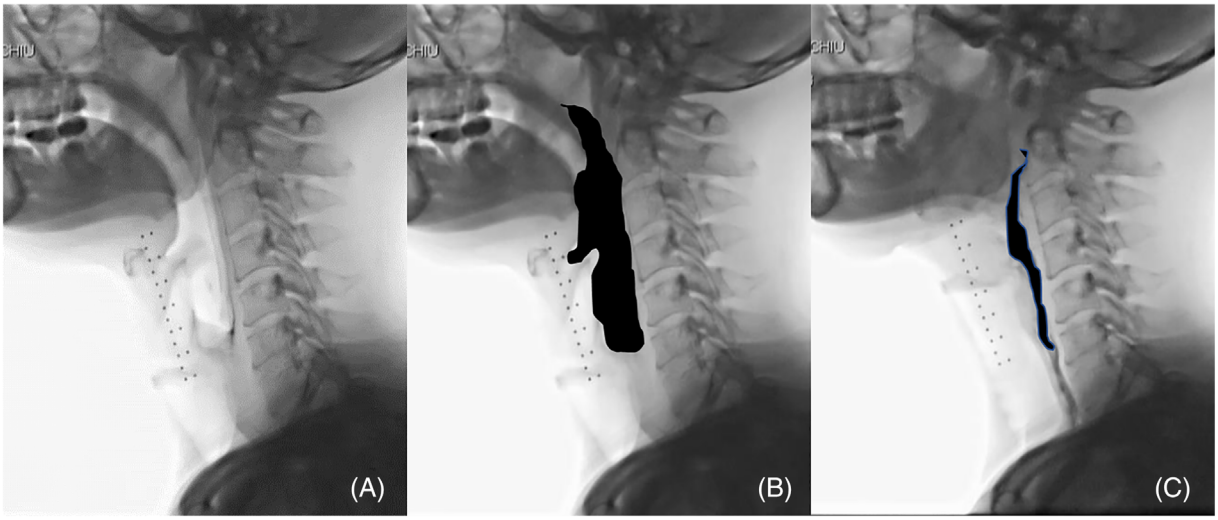

FIGURE 4 Measurement of the pharyngeal constriction ratio (PCR) on a videofluoroscopic study of swallowing. (A) The appearance of the pharynx at rest. (B) The cross-sectional area (X^2) of the oropharynx from the level of hard palate to the lower hypopharynx (black outline) before swallowing with a food bolus on hold in oral cavity. (C) The cross-sectional area (Y^2) of the oropharynx and hypopharynx (black outline) on maximal contraction during swallowing of the liquid barium contrast. The PCR is calculated by Y^2/X^2 with perfect contraction being 0 and absent contraction being 1 [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Characteristics of patients in the nasopharyngeal carcinoma and control groups

	Nasopharyngeal carcinoma	Control	*p* value
Number of cases	62	15	-
Age	59.55 ± 8.05	59.8 ± 9.84	0.917
Sex (male: female)	46:16	7:8	0.039
Average PCR	0.3378 ± 0.2273	0.027 ± 0.01547	<0.01
Vallecular residue	3.26 ± 0.79	1	<0.01
Pyriform fossa residue	3.56 ± 1.07	1.33 ± 0.49	<0.01
PAS	4.97 ± 2.06	1.4 ± 1.55	<0.01
VPSM (present: absent)	32:30	15:0	<0.01
EPCG	2.55 ± 1.26	1	<0.01
Aspiration (present: absent)	24:38	1:14	0.028

Abbreviations: EPCG, endoscopic pharyngeal contraction grading; PAS, penetration and aspiration scale; PCR, pharyngeal constriction ratio; VPSM, velopharyngeal squeeze maneuver.

significant results. For all statistical analyses, $p < 0.05$ was considered to be significant.

3 | RESULTS

3.1 | Demographic characteristics of patients

Seventy-seven patients were recruited into this study. Sixty-two patients (46 males and 16 females, mean age 59.5 years, range 44–78 years) with dysphagia after radiotherapy for nasopharyngeal cancer were recruited from three hospitals between 2015 and 2016. Thirty patients had previously had stage I or II nasopharyngeal carcinoma and 32 patients stage III or IV. Their mean duration after radiotherapy was 14 years (range 3–33 years), and their mean duration of dysphagia symptoms was 45.8 months (range 1–120 months). Sixteen patients had a history of aspiration pneumonia before their swallowing assessment. Fifteen patients (seven males and eight females, mean age 59.8 years, range 50–83 years) without symptoms of dysphagia and no history of radiotherapy were recruited as a control group. Table 2 summarizes the characteristics and major findings of swallowing function of the nasopharyngeal carcinoma and control groups.

TABLE 3 PCR values for an absent and present VPSM

VPSM	*N*	Mean PCR	SD	SE	95% confidence interval for mean	Minimum	Maximum
Absent	30	0.4744	0.18800	0.03432	0.40–0.54	0.07	0.75
Present	47	0.1514	0.17350	0.02531	0.10–0.20	0.01	0.67
Total	77	0.2772	0.23843	0.02717	0.22–0.33	0.01	0.75

Abbreviations: *N*, number; PCR, pharyngeal constriction ratio; SD, standard deviation; SE, standard error; VPSM, velopharyngeal maneuver (Mann-Whitney *U* test, $p < 0.05$).

TABLE 4 PCR values for differing EPCG

EPCG	*N*	Mean PCR	SD	SE	95% confidence interval for mean	Minimum	Maximum
Normal	34	0.0991	0.12512	0.02146	0.06–0.14	0.01	0.54
Mild	12	0.2156	0.11027	0.03183	0.15–0.29	0.03	0.37
Moderate	9	0.3512	0.21256	0.07085	0.19–0.51	0.09	0.59
Severe	22	0.5558	0.14270	0.03042	0.49–0.62	0.24	0.75
Total	77	0.2772	0.23843	0.02717	0.22–0.33	0.01	0.75

Abbreviations: EPCG, endoscopic pharyngeal contraction grading; *N*, number; PCR, pharyngeal constriction ratio; SD, standard deviation; SE, standard error (Kruskal-Wallis test, $p < 0.05$).

3.2 | Intra-rater and inter-rater reliability for the PCR, PSM, VPSM, EPCG scale, pharyngeal residue score, and PAS

During the FEES examination, the pharyngeal squeeze maneuver (PSM) was absent in 77 (100%) patients in which the VPSM was only absent in 30 (39%) of patients. ICC (ICC: 0.961, with 95% confidence interval [CI]: 0.943–0.974) suggested an excellent agreement for the three measured PCRs for each patient.

The intra-rater reliability of the three independent raters showed almost perfect agreement with the VPSM (Kappa coefficients: 0.948–1) and the PSM (Kappa coefficients: 0.922–1). The intra-rater reliability of the three raters also showed excellent reliability with the EPCG (ICC: 0.991–1), vallecular residue scores (ICC: 0.983–1), and pyriform residue scores (ICC: 0.987–1). On the one hand, the intra-rater reliability of the three raters also showed excellent reliability with the PAS (ICC: 0.994–1).

The inter-rater reliability between the senior otolaryngologist and the two independent raters for the VPSM was strong (Fleiss' Kappa coefficient: 0.88, with 95% CI: 0.76–0.96) but weak for the PSM (Fleiss' Kappa coefficient: 0.58, with 95% CI: 0.51–0.67).

Excellent reliability was also found between the three raters for the inter-rater reliability of the EPCG scale (ICC: 0.974, 95% CI 0.963–0.982), vallecular residue scores (ICC: 0.960, 95% CI 0.945–0.973), and pyriform residue scores (ICC: 0.962, 95% CI 0.945–0.974). On the other hand, excellent reliability was also found between the three raters for the inter-rater reliability of the PAS scale (ICC: 0.975, 95% CI 0.965–0.983).

3.3 | Correlation of the PCR with the VPSM and EPCG scale

There was a large but negative correlation between the PCR value and the VPSM, which was statistically significant ($r = -0.665$, $p < 0.05$). An absent VPSM was associated with a greater PCR value (Table 3). On the other hand, there was also a large and positive correlation between the PCR value and pharyngeal contraction when the PCR value increased with severity of impairment in pharyngeal contraction as rated by the EPCG scale, which was also statistically significant (Table 4) ($r = 0.812$, $p < 0.05$).

3.4 | Ordinal logistic regression of the VPSM and the EPCG scale

Ordinal logistic regression suggested that the VPSM is statistically significant in predicting impairment of pharyngeal contraction as rated by the EPCG scale with the Wald statistic = 29.99 and $p < 0.001$. Patients with an absent VPSM were more likely to have severe impairment of their pharyngeal contraction compared to patients with a present VPSM, with an odds ratio of 19.02 (95% CI: 6.63–54.56, $p < 0.001$).

TABLE 5 Yale pharyngeal residue scores for valleculae and pyriform fossae for different grades of velopharyngeal squeeze maneuver (VPSM) and endoscopic pharyngeal contraction grade (EPCG)

VPSM vs residue scores[a]								
	VPSM	***N***	**Mean scores**	**SD**	**SE**	**95% confidence interval for mean**	**Minimum**	**Maximum**
Vallecular residue	Absent	30	3.43	0.82	0.149	3.13–3.74	1	5
	Present	47	2.43	1.16	0.169	2.09–2.76	1	5
	Total	77	2.82	1.14	0.130	2.56–3.08	1	5
Pyriform residue	Absent	30	3.83	0.95	0.173	3.48–4.19	2	5
	Present	47	2.68	1.34	0.195	2.29–3.07	1	5
	Total	77	3.13	1.32	0.151	2.83–3.43	1	5
EPCG vs residue scores[b]								
	EPCG	***N***	**Mean scores**	**SD**	**SE**	**95% confidence interval for mean**	**Minimum**	**Maximum**
Vallecular residue	Normal	34	2.00	1.07	0.18	1.63–2.37	1	4
	Mild	12	3.17	0.72	0.21	2.71–3.62	2	4
	Moderate	9	3.33	0.50	0.17	2.95–3.72	3	4
	Severe	22	3.68	0.72	0.15	3.36–4.00	3	5
	Total	77	2.82	1.14	0.13	2.56–3.08	1	5
Pyriform residue	Normal	34	2.03	0.87	0.15	1.73–2.33	1	4
	Mild	12	3.83	0.94	0.27	3.24–4.43	2	5
	Moderate	9	3.56	1.01	0.34	2.78–4.33	2	5
	Severe	22	4.27	0.77	0.16	3.93–4.61	3	5
	Total	77	3.13	1.32	0.15	2.83–3.43	1	5

Abbreviations: *N*, number of patients; SD, standard deviation; SE, standard error.
[a]Mann-Whitney *U* test was used to test the pairs both show significant difference, $p < 0.05$.
[b]Kruskal-Wallis test, $p < 0.05$.

3.5 | Comparison and ordinal logistic regression of VPSM and EPCG to pharyngeal residue

Ordinal logistic regression showed that an absent VPSM was associated with an increase in the odds of having a more severe vallecular residue rating (odds ratio: 5.86, with 95% CI: 2.29–15.02, $p < 0.001$) and pyriform residue rating (odd ratio: 5.28, with 95% CI: 2.17–12.83, $p < 0.001$). There were statistically significant differences between impairment of pharyngeal contraction rated using the EPCG scale and the severity ratings of residue in the valleculae and pyriform fossae, respectively (Kruskal-Wallis test, $p < 0.05$). Using ordinal logistic regression and "normal" grading as the reference category, the results suggested that patients having "mild," "moderate," and "severe" gradings on the EPCG scale for pharyngeal contraction were associated with an increase in the odds of having a more severe rating of residue in the vallecula. The respective odds ratio values are 10.74 (95% CI 2.59–44.44, $p = 0.001$), 15.13 (95% CI 3.10–73.77, $p = 0.001$), and 35.43 (95% CI 9.21–136.30, $p < 0.001$). A similar association with the ECPG scale was also found with pyriform residue. The odds ratio values of "mild," "moderate," and "severe" are 40.99 (95% CI 8.66–194.11, $p < 0.001$), 21.71 (95% CI 4.38–107.73, $p < 0.001$), and 99.84 (95% CI 22.59–441.33, $p < 0.001$), respectively. Table 5 summarizes the severity of pharyngeal residue in the vallecula and pyriform fossa for different categories of the VPSM and gradings of the EPCG scale.

3.6 | Correlation of the VPSM and EPCG scale with aspiration

Twenty-five (32.5%) patients had aspiration in which 34 (44.2%) patients had penetration. To assess whether pharyngeal contraction and velopharyngeal squeeze can predict aspiration, binary logistic regression was used and suggested that an absent velopharyngeal squeeze was a statistically significant factor in positively predicting aspiration, with an odds ratio of 3.70 (95% CI 1.36–10.06,

$p = 0.01$). On the other hand, pharyngeal contraction of a "moderate" or "severe" grade rated by the EPCG scale was also statistically significant for positively predicting aspiration. The odds ratio for developing aspiration for "moderate" and "severe" ECPG grades in patients is 12.92 (95% CI 2.20–75.84, $p = 0.005$) and 22.14 (95% CI 5.01–97.89, $p < 0.001$), respectively, when the "normal" grading was used as the reference category.

4 | DISCUSSION

Aspiration pneumonia is a potentially fatal condition that can occur in patients who suffer from long-term dysphagia with aspiration and occurs in 23.8%–86% of patients who receive radiotherapy for nasopharyngeal carcinoma and has an associated mortality rate of 21%–76.9%.[27–30] In our previous study, we showed that pharyngeal contraction and stasis are two factors that correlate with the risk of aspiration in patients who suffer from dysphagia after radiotherapy for nasopharyngeal carcinoma.[13] The gold standard of measurement of pharyngeal motor function is pharyngeal manometry. Pharyngeal transit time can be measured during a VFSS examination. Leonard et al. proposed the application of the PCR to measure the pharyngeal contraction during VFSS, which is an objective measurement of the pharyngeal motor function, and which has been vigorously validated by pharyngeal manometry with a high intra-rater and inter-rater reliability.[23] The PCR has been shown to be highly predictive for aspiration, with patients three times more likely to experience aspiration when the ratio is higher than 0.25.[31] A present or absent PSM found during endoscopic examination also shows a statistically significant difference in the PCR values and is a useful objective sign to predict pharyngeal motor function.[16] However, the PSM is not a sign that can be commonly elicited in Chinese subjects as was shown by its complete absence in our study cohort including control subjects irrespective of their swallowing condition.

Velopharyngeal closure is important to seal off the oropharynx from the nasal cavity during swallowing to prevent leakage of intraoral pressure when the tongue pushes the food bolus into the pharynx with a piston movement.[15,32] This velopharyngeal closure can also be elicited during the production of a high-pitched sound with a low nasal tone. It should be present in all subjects irrespective of their ethnicity, language, or dialect. Velopharyngeal incompetence with hyper-nasality and nasal regurgitation can occur when velopharyngeal closure is impaired. The medial component of movement of the lateral wall of the velopharynx during velopharyngeal closure is defined as velopharyngeal squeeze in this study and can be used to predict pharyngeal motor function as a surrogate of the PSM of the hypopharynx. Our study demonstrated a significant difference in the mean PCR values between those subjects with a present or an absent VPSM observed during endoscopic swallowing examination when they were asked to phonate a forceful and high pitch "ee" vowel. The average PCR value for patients with the presence of VPSM is 0.15, which does not exceed 0.25, a cut-off limit of a "normal" PCR when the corresponding pharyngeal clearing pressure should be greater than 60 mm Hg, a normal cut-off value, according to one fluoroscopic and manometric study.[24] It also correlates with the impairment of pharyngeal contraction using the EPCG scale. Moreover, a present VPSM is also a statistically significant factor that predicts aspiration and more severe pharyngeal food residue in our subjects in this study. It can be used as a screening test during a FEES examination in Chinese patients to predict the pharyngeal motor function and risk of swallowing complications.

The EPCG scale has been used by the first author to rate the pharyngeal motor function of patients by employing the concept of the pharyngeal squeeze maneuver, which utilizes the aryepiglottic fold as an anatomical landmark to assess the degree of medialization of the lateral pharyngeal wall during contraction of pharyngeal muscles. Patients who suffer from dysphagia after radiotherapy tend to have a slow and impaired pharyngeal contraction and soft palate elevation, which allows the examiner a good appreciation of the movement of the lateral pharyngeal wall for EPCG rating purposes. Using the PCR as the gold standard for comparison of the values of different grades of the EPCG scale has demonstrated statistically significant differences among "normal," "mild," "moderate," and "severe" impairment grades, which confirms that the scale can demonstrate a gradation of impairment. Moreover, the PCR values for "normal" and "mild" impairment grades on the EPCG scale in this study did not exceed 0.25, which is the cut-off value for a normal PCR in the literature,[24] which was in contrast to the "moderate" and "severe" impairment grades where the PCR values were greater than 0.25. This demonstrated that the rating on the EPCG scale is not limited to its correlation with the PCR but is also able to predict the severity of pharyngeal motor function as the PCR values imply. The ECPG scale has also been shown to be able to predict the severity of food residue in the pharynx and risk of aspiration, which is consistent with the findings of our previous study of nasopharyngeal cancer subjects where pharyngeal motor function and stasis were two significant factors that predicted aspiration risk.[13]

This is the first study to report on the evaluation of pharyngeal motor function using a novel VPSM and a novel EPCG scale during a FEES. The intra-rater and

inter-rater reliability are important to determine the consistency of ratings using the VPSM and EPCG scale and of the feasibility of applying it to an endoscopic swallowing assessment of pharyngeal motor function. The Cohen's Kappa coefficients have demonstrated almost perfect agreement for the intra-rater reliability between the three raters, in which Fleiss' Kappa coefficient demonstrated strong agreement between the three raters for the VPSM. ICCs showed excellent reliability for the EPCG scale for the intra-rater and inter-rater reliability between the three raters. This is in contrast to the PSM in which the inter-rater reliability is weak between the three raters despite an almost perfect intra-rater reliability. This inconsistency may be due to the requirement for the lateral pharyngeal wall of the pyriform fossa to abut the aryepiglottic fold (AE) before the PSM is considered present. Most subjects were able to medialize the lateral pharyngeal wall to a small degree, but rarely did it touch the AE fold to create a present PSM. None of the subjects in this cohort of nasopharyngeal carcinoma and controls showed a present PSM. Therefore, the clinical value of PSM to predict pharyngeal motor function in Chinese subjects is not as useful as in a western population. On the other hand, both the VPSM and ECPG are easy to learn and had an exceptionally good intra-rater and inter-rater reliability when applied to Chinese subjects for assessment of pharyngeal motor function.

A limitation of this study was that the VPSM and EPCG scale were not tested in subjects with asymmetrical pharyngeal wall movement such as in patients with an ipsilateral pharyngeal paralysis or unilateral vocal cord palsy in which they represent a small number of cases in our clinic. Therefore, the interpretation of findings in terms of the prediction of pharyngeal residue and aspiration in those cases may require further study. Moreover, both the VPSM and EPCG scale only rated the range of movement of the lateral pharyngeal wall, making the assumption that the movement correlated with muscle strength and, hence, with muscle motor function. The odds ratio values to express the correlations between severity of pharyngeal residue/aspiration and different ratings of VPSM/EPCG showed wide confidence intervals, which may suggest poor precision in their estimation. Furthermore, the FEES and VFSS should ideally be performed on the same day. We allowed the time lag between the FEES and VFSS of up to 4 weeks due to limitations of resources for swallowing research. However, the nasopharyngeal carcinoma subjects that we recruited in this study had chronic dysphagia from an average of 14 years after radiotherapy and had swallowing symptoms for an average of 45.8 months. No subject with a post-radiotherapy duration of less than 12 months was recruited, when acute toxicities after treatment may still be existing. Therefore, any changes in swallowing function should not be significant in our subjects even though a lag time of up to 4 weeks existed between the FEES and VFSS examinations. All patients were screened by both an otolaryngologist and speech therapist to detect any subjective changes in swallowing function between the FEES and the VFSS to ensure consistency throughout the examinations. Finally, VFSS recorded at 15 frames/s may not be able to pick up changes in swallowing physiology that recording at 30 frames/s might. Recording a VFSS at 15 frames/s is standard in our center where we aim to balance the exposure of our patients to radiation during the VFSS and the efficacy of the examination to pick up swallowing pathology. The literature has shown that recording a VFSS at 15 frames/s does not affect the detection of penetration and aspiration the during swallowing examination, which is consistent with our experience in clinical practice.[33] Similarly, our study demonstrated that recording a VFSS at 15 frames/s does not affect the estimation of the PCR during swallowing in the control subjects without dysphagia, with a mean value approaching zero, which is another new and important finding that comes from this study.

5 | CONCLUSIONS

The VPSM is predictive of pharyngeal motor impairment in the Chinese post-irradiated nasopharyngeal carcinoma patient study group, as is the pharyngeal squeeze maneuver in western patients, and the EPCG scale is a simple, useful, and reliable tool for use during a flexible endoscopic evaluation of swallowing. Both the VPSM and EPCG scale statistically predicted the severity of food residue in the pharynx and the risk of aspiration in the study group. Further evaluation of these is needed to validate their applicability to other disease entities and other ethnic groups.

DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions

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